Effect of lipid-modifying drug therapy on survival after abdominal aortic aneurysm repair

Gaurav M. Parmar, MD, MPH, Bruce Lowman, MD, Bart R. Combs, MD, Steve M. Taylor, MD, Mark A. Patterson, MD, Marc A. Passman, MD, and **William D. Jordan Jr, MD, FACS,** *Birmingham, Ala*

Background: **Lipid-modifying drug therapy (LMDT) is recommended in all patients having coronary or noncoronary atherosclerotic disease. However, the effect of LMDT after abdominal aortic aneurysm (AAA) repair, especially in the absence of other atherosclerotic manifestations, is unclear. We examined the distribution of prevalence of LMDT among patients undergoing AAA repair and its effect on survival in the presence and absence of other atherosclerotic diseases.**
Methods: **We identified patients treated at University of Alabama at Birmingham between 1985 and 2010 who had a prior AAA repair. Information was collected from health system medical charts, medical communication, and national death indices. We assessed the predictors of prevalence of LMDT by univariate analysis using *t*-test for continuous and χ^2 test for categorical variables, and then performed multivariate logistic regression. The survival was determined using Kaplan-Meier plots, and adjusted hazard ratios were calculated using Cox proportion regression.**
Results: **A total of 2063 patients underwent AAA repair procedure. Of these, 9% were African-American, and 20% were female. Thirty-five percent received LMDT, and 32% died during the follow-up period of up to 240 months. Significant predictors for being on LMDT included white race (odds ratio [OR], 1.6; 95% confidence interval [CI], 1.1-2.2), presence of other atherosclerotic disease or diabetes (OR, 2.4; 95% CI, 1.9-3.0), hypertension (OR, 4.0; 95% CI, 3.1-5.2), smoking (OR, 1.6; 95% CI, 1.2-2.1), and endovascular AAA repair (OR, 1.9; 95% CI, 1.5-2.3). LMDT was associated with improved survival (hazard ratio, 0.6; 95% CI, 0.5-0.8) after controlling for traditional risk factors, diabetes, and other atherosclerotic diseases.**
Conclusions: **LMDT after AAA is associated with an increased survival compared with patients who were not using drug therapy for dyslipidemia. Aggressive management of dyslipidemia should be considered in all patients undergoing AAA repair irrespective of other atherosclerotic disease status and risk factor profile. (J Vasc Surg 2013;58:355-63.)**

Each year, approximately 57,000 hospital discharges and nearly 19,000 deaths occur in individuals with abdominal aortic aneurysms (AAA) in the U.S.[1] The 2005 collaborative report from the American College of Cardiology Foundation, American Heart Association, Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Interventional Radiology (hereafter, "PAD task force") on practice guidelines for the management of patients with peripheral arterial disease (PAD; lower extremity, renal, mesenteric, and abdominal aortic) defines AAA when the anteroposterior diameter of the aorta is more than or equal to 3.0 centimeters.[2] The prevalence of small AAA (3.0-4.9 cm in diameter) ranges from 1.3% in younger men (aged 45-54 years) to 12.5% in older men (aged 75-84 years), and 0% to 5.2% in the respective women categories.[1,2] Large AAA (≥5 cm in diameter) expand more rapidly than small AAA, and carry a higher risk for rupture that may be associated with death rates as high as 90%.[1,2]

Lipid-modifying drug therapy (LMDT) is recommended in all patients having coronary heart disease or having clinical manifestations of any noncoronary forms of atherosclerotic disease.[2-4] Prescription of statin as a cholesterol lowering agent for protection from myocardial infarction, stroke, and cardiovascular death in patients with PAD was introduced as a performance measure in the 2010 collaborative report from the PAD task force.[5] However, the effect of LMDT on survival after AAA repair, especially in the absence of other atherosclerotic manifestations, is unclear. In a recently conducted systemic review and meta-analysis of the effects of statins on AAA, Twine et al[6] were unable to identify conclusive evidence for reduction in mortality after rupture,[7] improved survival free from AAA repair,[8] and cardiovascular specific mortality[9]; mostly because these outcomes were either not reported separately or were available only in single studies. They also concluded that the statins had no effect on AAA expansion.[6] Higher levels of triglycerides and low-density lipoprotein (LDL) cholesterol were not associated with increased risk of AAA in an Australian study.[10]

Possible biological mechanisms for this relationship seem to be multifaceted. AAA formation involves chronic inflammation, depletion of smooth muscle cells, and increased degradation of aortic wall proteins by matrix metalloproteinases (MMP).[11,12] An imbalance between MMP

From the Section of Vascular Surgery and Endovascular Therapy, University of Alabama at Birmingham.
Author conflict of interest: none.
Presented at the Thirty-sixth Annual Spring Meeting of the Peripheral Vascular Surgery Society, Chicago, Ill, June 15, 2011.
Reprint requests: Gaurav M. Parmar, MD, MPH, Section of Vascular Surgery and Endovascular Therapy, University of Alabama at Birmingham, 1808 7th Ave S, Birmingham, AL 35294 (e-mail: Drgaurav80@gmail.com).
The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.
0741-5214/$36.00

http://dx.doi.org/10.1016/j.jvs.2013.01.036

and their tissue inhibitors is implicated in aneurysmal disease.[13] Statins have pleiotropic effects, including anti-inflammatory activity, apart from their cholesterol-lowering action.[14] There is some observational evidence that statins reduce MMP concentrations in the AAA wall,[13,15,16] including few case-series demonstrating the association between statin prescription and reduced AAA growth.[17-19] However, a recent randomized controlled trial conducted by Rahman et al found that statin use does not influence the levels of MMP or their inhibitors in AAA wall.[20] Moreover, statin use was associated with increased risk of AAA in a recent large population-based observational (Tromsø) study.[21] The Tromsø study also concludes that atherosclerosis may not be a causal event in AAA but develops in parallel with or secondary to aneurysm.[22] As a result of lack of substantial evidence, the 2005 Society for Vascular Surgery practice guidelines for the management of patients with peripheral arterial disease suggest that it remains to be determined whether statin therapy could be useful for prevention or treatment of AAA.[2]

The University of Alabama at Birmingham Vascular registry provides this unique opportunity to study the short- and long-term effects of LMDT on AAA repair. We agree with Twine et al that it is relatively unlikely to have a randomized controlled trial in the future to specifically answer the question of whether all patients with AAA should be on LMDT for cardiovascular protection.[6] We examined the distribution of LMDT prevalence among patients undergoing AAA repair and its effect on survival from aneurysm-related mortality, cardiovascular-specific mortality, and all-cause mortality in the presence and absence of diabetes and other atherosclerotic diseases.

METHODS

Study design and participants. We identified index atherosclerotic AAA repair procedures performed between 1985 and 2010 at the University of Alabama at Birmingham vascular surgery service from a prospectively maintained registry (Fig 1). Procedures performed due to nonatherosclerotic reasons such as trauma, mycotic aneurysms, and collagen vascular diseases were excluded. Information was collected from health system medical charts, including discharge summaries, operative reports, laboratory data, outpatient clinic visits, medical communications, and Social Security Death Index (SSDI) website. Demographic factors included age, gender, and race. Prior to surgery, patients were screened for risk factors, including smoking, coronary artery disease, hypertension, carotid disease, lower extremity atherosclerotic disease, chronic pulmonary disease, stroke, diabetes, and renal dysfunction. The study protocol was reviewed and approved by the University of Alabama Institutional Review Board.

Definition of variables. Age was categorized into 10-year intervals of <55, 55-64, 65-74, 75-84, and ≥85; racial grouping was either African-American or White. Smoking was categorized as currently smoking, past smoking (but not currently), or never having been a smoker based upon patients' history. Coronary artery disease was defined as patient report, physician diagnosis report in the medical records or communications, or a history of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting. Hypertension was defined as having been previously diagnosed with hypertension, or treatment with antihypertensive medications. Carotid and lower extremity atherosclerotic diseases were identified through screening of vascular registry if participants had any clinic visits, hospital admissions, or procedures performed for these vascular conditions. Chronic obstructive pulmonary disease and stroke were defined as physician diagnosis report in the medical records or communications, or via imaging evidence. Diabetes was defined as having been diagnosed with diabetes, or treatment with insulin, or on oral anti-diabetic medications. Treatment with dialysis was used as a surrogate for end-stage renal dysfunction. To study the role of coronary heart disease risk-equivalent as defined in the Adult Treatment Panel (ATP) III guidelines of the National Cholesterol Education Program (NCEP), we created a composite variable as presence of other atherosclerotic disease or diabetes. Other atherosclerotic diseases included coronary artery disease, lower extremity atherosclerotic disease, and carotid disease.

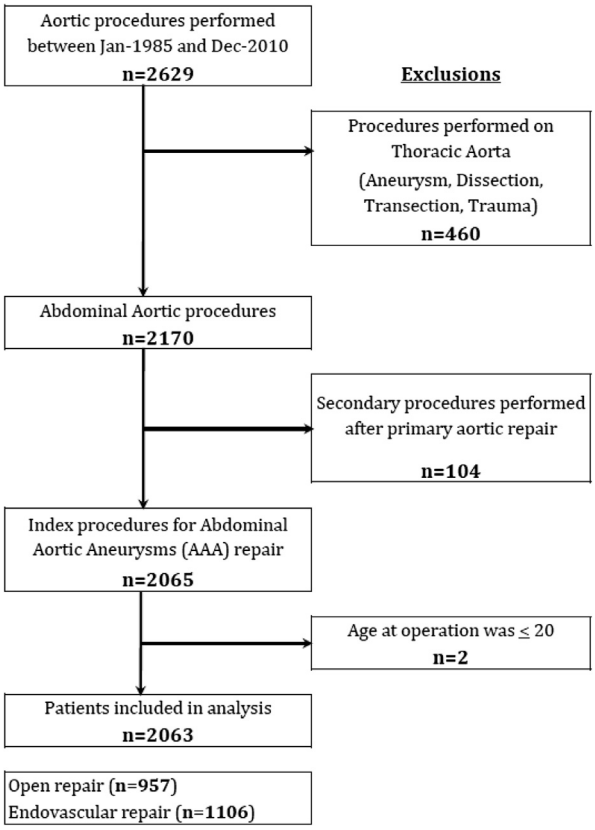

Fig 1. Identification of eligible study participants.

Use of LMDT. The University of Alabama at Birmingham vascular surgery service protocol requires patients to visit the outpatient clinic within 4 weeks after a major vascular procedure, and every 6 to 12 months thereafter. In case of a loss to follow-up, the patient's primary care provider is contacted by telephone. LMDT may have been initiated for higher LDL, higher triglycerides, lower high-density lipoprotein cholesterol, or as a part of NCEP's ATP III recommendations for the primary prevention of myocardial infarction and cardiovascular death.[4] LMDT includes patients taking stains as well as any lipid-lowering drug therapy other than therapeutic lifestyle changes, including fibrates (gemfibrozil, fenofibrate), bile acid sequestrants (cholestyramine, colestipol, and colesevelam), cholesterol absorption inhibitors (ezetimibe), or nicotinic acid.

Outcomes. Vital status information was ascertained by reviewing registry records and via SSDI.[23] Patients were censored at the time of death or at the last clinic correspondence to our vascular service in the time-to-event analyses. Cause of death was determined from the hospital record for patients who died during follow-up at University of Alabama Vascular service, and by contacting relatives and/or primary care provider for those who died outside of the hospital. Death was classified as "unknown" if it was ascertained through SSDI without further information or when the cause of death was uncertain. The main outcomes of the study were all-cause and aneurysm-related mortality. All deaths within 30 days of aneurysm repair were considered to be related to the aneurysm. As part of a sensitivity analysis, deaths due to nonaortic vascular causes (stroke, carotid, or lower extremity) and deaths related to cardiac causes (myocardial infarction, heart failure, arrhythmia, or sudden death) were combined with aneurysm-related deaths to create a cardiovascular mortality group.

Statistical analysis. We assessed the predictors of prevalence of LMDT by univariate analysis using Student *t*-test for continuous variables and χ^2 test for categorical variables. We then performed multivariable logistic regression to determine the strength of association for significant variables. The survival was determined using Kaplan-Meier plots, and adjusted hazard ratios were calculated using Cox proportion regression. Differences between survival curves were compared with the log-rank test. In analyses of aneurysm-related mortality and cardiovascular mortality, patients who died of nonaneurysmal causes and noncardiovascular causes, respectively, were censored at the time of death. Statistical significance was set at an alpha value of 0.05. All statistical analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

A total of 2629 aortic procedures were performed between January 1985 and December 2010 at the University of Alabama at Birmingham Vascular Surgery service. Of these 2629 procedures, 460 were performed on thoracic aorta for various reasons and were excluded from the current study. We also excluded 104 aortic procedures performed secondarily after primary aortic repair procedure. Thus, we identified 2065 index procedures for AAA repair (Fig 1). Two procedures were excluded because they were performed in patients younger than 20 years of age; one was a 6-year-old African American girl who underwent open AAA repair in 2008, and the other was a 9-year-old Hispanic boy with a mycotic aneurysm that had been denied open repair and required an endovascular repair in 2009.

Of the 2063 patients who underwent index AAA repair procedure, 35% (n = 726) received LMDT and 32% (n = 656) died during the follow-up period of 241 months. In comparison to patients who did not use LMDT, the LMDT users were smokers (87% vs 61%; $P < .0001$) and more often whites (92% vs 78%; $P = .03$), and had a higher prevalence of hypertension (86% vs 48%; $P < .0001$), diabetes (19% vs 8%; $P = .0001$), and other atherosclerotic diseases (75% vs 44%; $P < .0001$; Table). Multivariable adjusted logistic regression revealed that hypertension (odds ratio [OR], 4.0; 95% confidence interval [CI], 3.1-5.2) was the strongest predictor for patients being on LMDT, followed by presence of other atherosclerotic diseases or diabetes (OR, 2.4; 95% CI, 1.9-3.0), and endovascular repair (OR, 1.9; 95% CI, 1.5-2.3). White race was a significant predictor for being on LMDT (OR, 1.6; 95% CI, 1.1-2.2) compared with African Americans, which supports past reports.[24] Smokers were also more likely to be on LMDT (OR, 1.6; 95% CI, 1.2-2.1) than nonsmokers.

The mean follow-up was 31 months (range, 0 to 241 months). Of the 656 patients (32%) who died during follow-up, 82 (13%) died due to aneurysm-related causes, and an additional 49 (7%) died due to cardiac or other nonaortic vascular causes. Cardiovascular mortality included aneurysm-related, cardiac, and nonaneurysm-related vascular mortality (82 + 49 = 131). Most of the patients died from causes unrelated to aneurysm or cardiovascular disease process. The cause of death was unknown for patients whose deaths were identified through SSDI. Patients who died had a longer mean follow-up compared with those who did not die (40 months vs 27 months). Similarly, patients with presence of other atherosclerotic disease or diabetes had slightly longer mean follow-up compared with those without them (35 months vs 26 months). However, mean follow-up did not differ by type of AAA repair procedure (32 months for open repair vs 31 months for endovascular repair).

LMDT users had significantly improved survival from aneurysm-related mortality at 30 days (98.1 % vs 94.7%), 1 year (98% vs 94.5%), and 5 years (98% vs 94.5%) compared with nonusers (standard error [SE], <10%; log-rank *P* value = .0001; Fig 2, *a*). There was more obvious improvement in survival from all-cause mortality among LMDT users at 30 days (98.1% vs 94.7%), 1 year (90% vs 84.6%), and 5 years (68.5% vs 51.6%) compared with nonusers (SE, <10%; log-rank *P* value < .0001; Fig 2, *c*). In sensitivity analysis for cardiovascular mortality,

Table. Baseline characteristics (n = 2063 patients)

	Lipid-modifying drug therapy				
	No (n = 1337)		*Yes (n = 726)*		
	No.	*%*	*No.*	*%*	P *value*
Demographics:					
Age					
<50 years	100	7.5	23	3.2	.14
51-64 years	275	20.6	160	22.0	
65-74 years	568	42.5	331	45.6	
75-84 years	345	25.8	197	27.1	
>85 years	49	3.7	15	2.1	
Male gender	1039	77.7	617	85.0	.26
Race					
African-American	131	9.8	58	8.0	.03[a]
European-American	1048	78.4	664	91.5	
Other	158	11.8	4	0.6	
Risk factors:					
Diabetes	103	7.7	136	18.7	.0001[a]
Hypertension	639	47.8	625	86.1	<.0001[a]
Ever smoker	819	61.3	631	86.9	<.0001[a]
Chronic obstructive pulmonary disease	283	21.2	162	22.3	.88
Dialysis	34	2.5	26	3.6	.28
Other atherosclerotic diseases	592	44.3	544	74.9	<.0001[a]
Coronary artery disease	492	36.8	499	68.7	<.0001[a]
Stroke	123	9.2	90	12.4	.02[a]
Carotid disease	36	2.7	35	4.8	.01[a]
Lower extremity arterial disease	69	5.2	55	7.6	.03[a]
Other atherosclerotic diseases or diabetes	627	46.9	569	78.4	<.0001[a]
AAA repair type					
Open repair	703	52.6	254	35.0	<.0001[a]
Endovascular repair	634	47.4	472	65.0	

AAA, Abdominal aortic aneurysm.
Student *t*-test used for continuous variables and χ^2 test used for categorical variables.
[a]Statistical significance was set at alpha of .05.

they also had significantly improved survival at 30 days (98.1% vs 94.7%), 1 year (97.7% vs 93.3%), and 5 years (94.4% vs 90.3%) compared with nonusers (SE, <10%; log-rank *P* value = .0003; Fig 2, *b*). Survival estimates at different time intervals were obtained through life-table method. The association between LMDT and mortality remains unchanged after adjusting for other covariates in Cox proportional hazard regression. LMDT users had a 50% reduction in aneurysm-related mortality (HR, 0.5; 95% CI, 0.3-0.9), a 40% reduction in cardiovascular mortality (HR, 0.6; 95% CI, 0.4-0.9), and a 40% reduction in all-cause mortality (HR, 0.6; 95% CI, 0.5-0.8) after adjusting for age, race, gender, type of AAA repair, diabetes, hypertension, smoking, and presence of other atherosclerotic diseases (Fig 3).

Presence of other atherosclerotic disease or diabetes was not associated with aneurysm-related mortality (HR, 0.8; 95% CI, 0.5-1.3) or cardiovascular mortality (HR, 0.9; 95% CI, 0.6-1.3). However, this association was marginal for all-cause mortality (HR, 1.1; 95% CI, 1.0-1.4). Compared with open AAA repair, endovascular repair was protective for aneurysm-related mortality (HR, 0.4; 95% CI, 0.2-0.6) and all-cause mortality (HR, 0.7; 95% CI, 0.6-0.9), but failed to reach statistical significance for cardiovascular mortality (HR, 0.8; 95% CI, 0.5-1.1). White race was also protective for all three mortality groups: aneurysm-related (HR, 0.4; 95% CI, 0.2-0.6), cardiovascular (HR, 0.4; 95% CI, 0.3-0.7), and all-cause (HR, 0.7; 95% CI, 0.5-0.9). Age showed a clear linear trend of increase in all mortality (aneurysm-related, cardiovascular, and all-cause) with increasing age. Gender, hypertension, and smoking status were not associated with any of these mortality groups.

DISCUSSION

Aneurysm-related, cardiovascular, and all-cause mortality rates following AAA repair were significantly and independently improved by LMDT in the present study. Since ours is not a randomized study, LMDT users were different from nonusers in clinical characteristics. LMDT users had a higher prevalence of smoking, diabetes, hypertension, and other atherosclerotic diseases. The association between LMDT use and reduced mortality remained consistent after adjustment for demographics, traditional risk factors, and type of AAA repair.

Evidence-based recommendations on the management of dyslipidemia and related disorders are published periodically by NCEP's expert panel (ATP). The most recent revision of these recommendations was published in 2004,[4] while the earlier guidelines were published in 1988 (ATP I),[25] 1993 (ATP II),[26] and 2001 (ATP III).[27] According to the most recent guideline, the highest risk category (10-year risk of hard coronary heart disease [CHD] event >20%) includes CHD or CHD risk equivalents. Hard CHD events include myocardial infarction and CHD death. CHD risk equivalents include diabetes and clinical manifestations of noncoronary forms of atherosclerotic disease (PAD, AAA, stroke, and transient ischemic attacks of carotid origin). LDL cholesterol goal is <100 mg/dL (<70 mg/dL optional) in this risk category. However, LMDT benefits even when baseline LDL is average or normal.[28-33] According to this guideline, all of our registry patients who underwent AAA repair should receive LMDT. But inclusion of AAA as a CHD risk equivalent is relatively recent, whereas diabetes and atherosclerotic diseases were considered high-risk for hard CHD event from the very beginning. So, the presence of diabetes or atherosclerotic disease should be the strongest predictor of being on LMDT. In our registry, we found that hypertension is the strongest predictor of receiving LMDT.

Despite clearly demonstrated benefits of LMDT for cardiovascular protection in atherosclerotic diseases, its effect on pathophysiology of AAA still remains questionable. AAA and atherosclerosis are associated with each other.[34,35] However, it is unclear whether atherosclerosis causes AAA or vice versa.[35,36] In experimental models, aneurysm development preceded the atherosclerotic

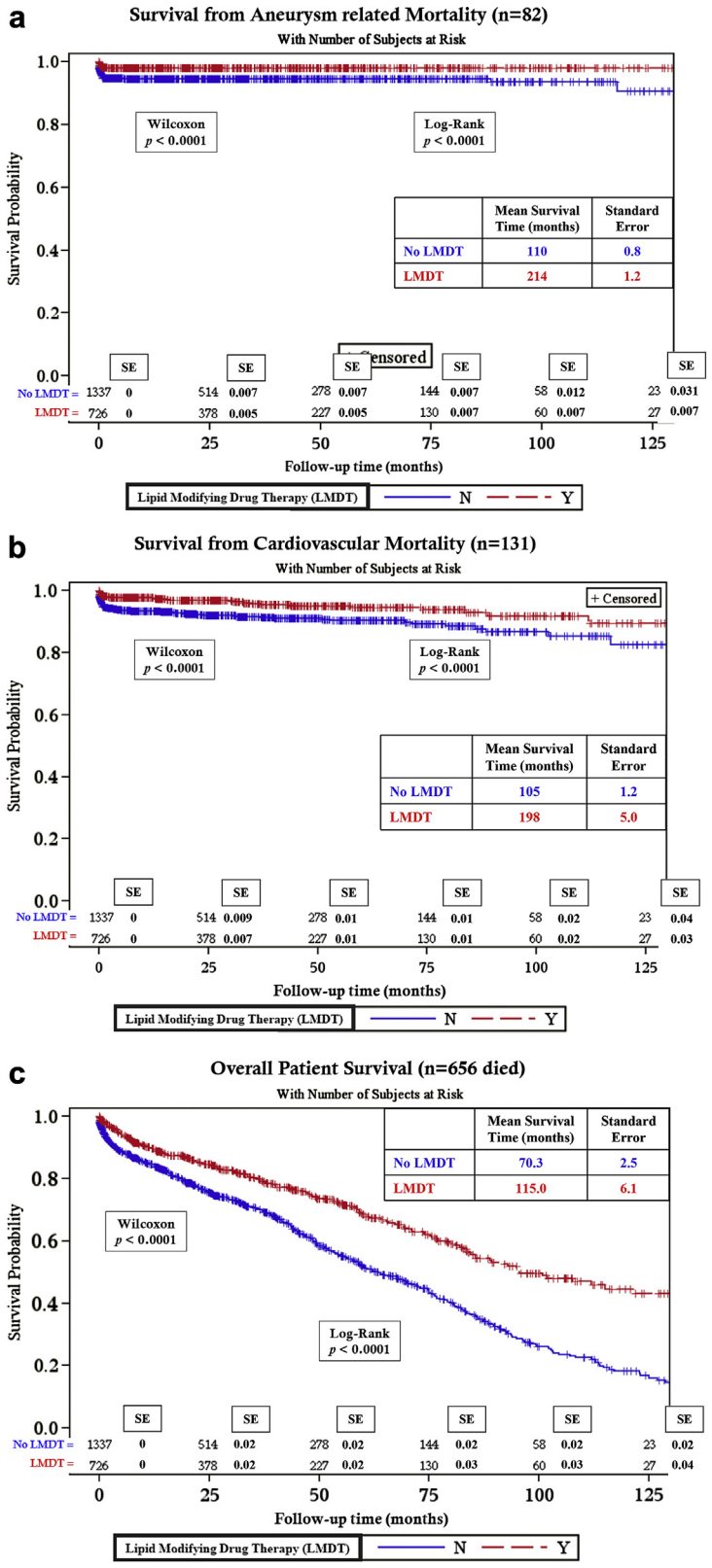

Fig 2. a, Survival from aneurysm-related mortality (n = 82). **b,** Survival from cardiovascular mortality (n = 131). **c,** Survival from all-cause mortality (n = 656). *LMDT,* Lipid-modifying drug therapy; *SE,* standard error.

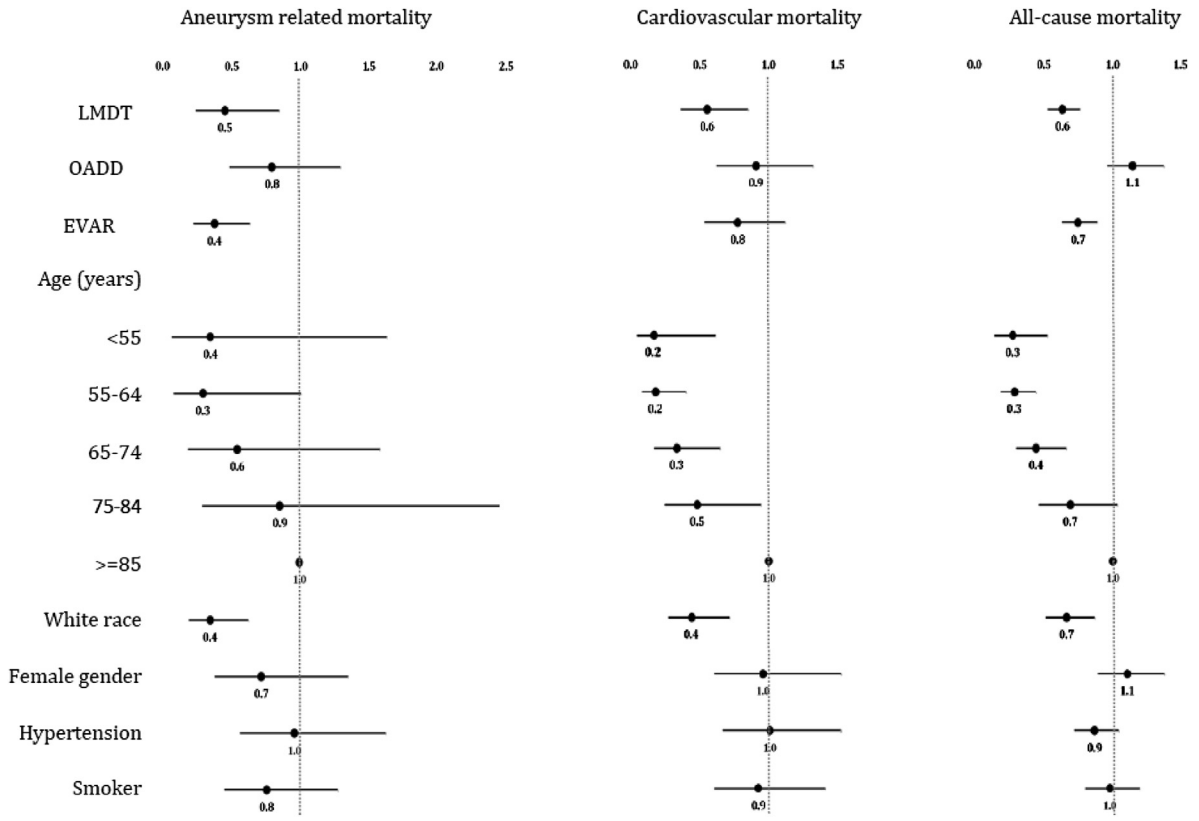

Fig 3. Multivariable adjusted hazard ratios with 95% confidence intervals (CIs) from Cox proportional hazard regression. *EVAR,* Endovascular repair; *LMDT,* lipid-modifying drug therapy; *OADD,* other atherosclerotic diseases or diabetes.

lesions.[37] One study even suggested that AAA develops in parallel with atherosclerosis and is not causal.[22] Our results demonstrate significant benefits in aneurysm-related mortality by LMDT even after adjustment for diabetes and atherosclerotic diseases. Possible mechanisms of this effect apart from atherosclerosis is unclear. Some studies showed that LMDT reduced MMP concentrations in the AAA wall,[13,15,16] including a few case series demonstrating the association between statin prescription and reduced AAA growth.[17-19] Statins attenuates plaque inflammation, influence plaque stability,[38] and affect the coronary and non-coronary circulation.[39] Statins suppress the development of AAA in mice[40,41] and reduce the risk of AAA rupture in humans.[8] Clear understanding of possible biological mechanisms of this effect still warrants further investigation.

Patients treated with endovascular repair are more likely to receive LMDT compared with patients treated with open repair in our registry. One can expect this, as LMDT in patients with symptomatic AAA is recommended by recently published ATP III guidelines, and endovascular repair is a relatively newer minimally-invasive alternative treatment for AAA. Some studies showed no survival benefit by type of repair procedure,[42] while others showed early survival benefit by endovascular repair, which was lost after 1 to 3 years.[43,44] However, we earlier showed that endovascular repair has survival benefit over open repair in an observational retrospective analysis for up to 9 years of follow-up.[45] This does not account for the effect of LMDT on mortality in adjusted analysis. LMDT and endovascular repair both independently improved survivals in our study.

Our study has several limitations to consider. Information regarding LMDT was collected dichotomously in the UAB vascular registry, with two possible entries being 'YES' or 'NO.' Therefore, we did not have information on which drug they were receiving and whether the drug therapy was effective in controlling their lipid levels or not. However, a recent revision of ATP III guideline suggests to correct all lipid disorders aggressively and not only LDL. It also suggests considering combinations of other drugs like fibrates and niacin with statins to achieve optimum lipid control. Since we do not have actual lipid levels in our registry, we were unable to comment on control of lipids. However, dyslipidemia in non-LMDT users is unlikely in our registry due to follow-up, and uncontrolled lipids in LMDT users would introduce bias towards null, which would ultimately underestimate the protective effect of LMDT. We also did not have information regarding when the LMDT was initiated with regard

to AAA repair. LMDT could have been initiated before, on the day of, or after AAA repair procedure. While the mortality benefit of LMDT is greatest in those patients who are on longer duration of treatment, benefits were noted in patients recently started on LMDT as well.[46] Because of the nature of this study, we do not have information about compliance for LMDT use. However, noncompliance of LMDT would introduce bias towards null and underestimate the protective effect of LMDT. Finally, we were unable to ascertain cause of death when a patient was lost to follow-up or when death was identified through SSDI. Nevertheless, the consistent survival benefit of LMDT across all mortality outcomes is noteworthy. As in all observational studies, caution in ascribing the observed effects to LMDT is prudent.

In conclusion, LMDT is independently associated with improved survival from aneurysm-related mortality, cardiovascular mortality, and all-cause mortality in patients who have completed AAA repair after adjusting for traditional risk factors, diabetes, and other atherosclerotic diseases. Aggressive management of dyslipidemia should be considered in all patients undergoing AAA repair irrespective of their other atherosclerotic disease status and risk factor profile.

AUTHOR CONTRIBUTIONS

Conception and design: GP, WJ
Analysis and interpretation: GP, WJ
Data collection: GP, BL, BC, ST, MPatterson, MPassman, WJ
Writing the article: GP, WJ
Critical revision of the article: GP, BL, BC, ST, MPatterson, MPassman, WJ
Final approval of the article: GP, BL, BC, ST, MPatterson, MPassman, WJ
Statistical analysis: GP, WJ
Obtained funding: WJ
Overall responsibility: GP, WJ

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Submitted Sep 19, 2012; accepted Jan 15, 2013.

DISCUSSION

Dr Matthew Mell (*Stanford, Calif*). I would like to thank the PVSS for the privilege of discussing this paper, and I would like to commend the research done by the group at Alabama looking at the value of statins for patients who receive aneurysm repair. I would also like to personally thank the authors for providing in advance a copy of the manuscript.

These findings that statin use is variable across different populations, and, additionally, that it is an independent predictor of survival adds to the growing body of literature emphasizing the importance of optimal medical management for patients with surgical vascular disease. Other studies have shown that cardiovascular risk reduction is not offered to many of the surgical patients with cardiovascular disease, and perhaps this study will highlight the importance of providing more complete care to our vascular patients who, as a rule, have significant coexisting disease.

I have three questions. First, your study showed improved survival even after controlling for underlying cardiovascular disease, suggesting that the statins may exert their effect beyond that of reducing death associated with cardiovascular disease. Do you think that this is likely a direct effect, or do you think that perhaps patients receiving statins are also more likely to receive better general care, for example, routine visits, cancer screening, and so forth?

Second, I'm wondering if you could elaborate a little more about the causes of death. In the manuscript, you described that about 20% of the deaths were attributed to either aneurysm-related causes or cardiovascular disease. How many of the remaining 80% were due to actual other causes and for how many were the causes not available because the deaths were collected from SSDI and therefore unknown? Do you think having more complete information regarding the cause of death would change your results?

My final question is, had you considered including aneurysm size in your analysis? Your institution has published on the feasibility of repairing small aneurysms, and other authors have suggested that there is a link between aneurysm size and mortality. It might be valuable to include this variable in your analysis.

Once again, thank you to the PVS and the authors. I look forward to your thoughts.

Dr Gaurav M. Parmar. Thank you so much for your really important comments.

Number one is the role of statins on abdominal aortic aneurysms. It is thought that the effects of statins are through usual atherosclerotic route by inhibiting HMG-Co-A reductase. There are relatively fewer studies that address other pathophysiologic mechanisms. There are a couple of clinical trials that tried to demonstrate the pleiotropic effects of statins on aortic wall stress by using different markers, but the evidence is iffy; it's not conclusive.

The second point, yes, about 20% of our deaths were attributed to aneurysm or cardiovascular events. Most of the remaining deaths either come from SSDI or are due to cancer or causes grouped as others. I would be very happy to provide the entire distribution of our causes of death. Using SSDI to identify deaths is a limitation of our study, and we do not have any other way to ascertain cause of death on those deaths. But still it is reasonable to attribute such a large mortality benefit effects to use of LMDT.

Third, aneurysm size; unfortunately, we did not look at aneurysm size in this analysis. I think that is an important consideration and we will look forward to that.

Dr James Reeves (*Atlanta, Ga*). I have one question. How do you at UAB handle initiating statin therapy on these patients? Do you initiate it yourself, or do you have a vascular medicine specialist in your department who follows these patients? If you do initiate it yourself, how do you follow the side effects, any adverse events, or titrate the dose?

Dr Parmar. We do have vascular medicine physicians at our institution. As I said, we don't know about when the lipid management was actively initiated. It could have been initiated by the primary care practitioner earlier, at the time of surgery by our group, or during postoperative follow-up visits.

Dr Mark A. Patterson. Thank you Dr Reeves, as one of the authors, I can address that.

At UAB, we have two vascular medicine physicians that assist with perioperative and postoperative medical management. If patients are not taking statins at the initial visit, those gentlemen become involved, and oftentimes initiate statins. That is not me the surgeon, but us the team. Specific communication is sent to the primary care doctor. I must say that it is uncommon for us to get a referral from either a UAB or outside physician, in which the patient is not already on a statin regimen. Unfortunately, I don't have a specific number, but it is not very large.